Application No.: NEW Docket No.: 5999-0525PUS3

## **AMENDMENTS TO THE CLAIMS**

## 1. (Original) A compound according to formula I

$$(R^{1})_{m}$$
 $P$ 
 $X^{2}$ 
 $X^{3}$ 
 $X^{4}$ 
 $Q$ 
 $(R^{2})_{n}$ 
 $(R^{2})_{n}$ 
 $(R^{2})_{n}$ 
 $(R^{2})_{n}$ 
 $(R^{2})_{n}$ 

wherein

P is selected from aryl and heteroaryl;

R¹ is attached to P via a carbon atom on ring P and is selected from the group consisting of hydroxy, halo, nitro, C¹-6alkylhalo, OC¹-6alkylhalo, C¹-6alkyl, OC¹-6alkyl, C²-6alkenyl, OC²-6alkenyl, C²-6alkynyl, OC²-6alkynyl, C²-6alkynyl, C³-6alkylC³-6cycloalkyl, OC¹-6alkylC³-6cycloalkyl, C³-6alkylC³-6cycloalkyl, C³-6alkylC³-6cycloalkylC³-6c

3

Application No.: NEW Docket No.: 5999-0525PUS3

X<sup>1</sup> is selected from the group consisting of: N, NR<sup>4</sup> and CR<sup>4</sup>;

X<sup>2</sup> is selected from the group consisting of: C and N;

X<sup>3</sup> is selected from the group consisting of: CR<sup>4</sup>, N and O;

X<sup>4</sup> is selected from the group consisting of: CR<sup>4</sup>, N, NR<sup>4</sup> and O;

X<sup>5</sup> is selected from the group consisting of: a bond, CR<sup>4</sup>R<sup>4</sup>, NR<sup>4</sup>, O, S, SO and SO<sub>2</sub>;

X<sup>6</sup> is selected from the group consisting of: CR<sup>4</sup> and N;

X<sup>7</sup> is selected from the group consisting of: C and N;

 $R^4$  is independently selected from a group consisting of hydrogen, hydroxy,  $C_{1-6}$ alkyl,  $C_{0-6}$ alkylcyano, oxo, =N $R^5$ , =NO $R^5$ ,  $C_{1-4}$ alkylhalo, halo,  $C_{3-7}$ cycloalkyl, O(CO) $C_{1-4}$ alkyl,  $C_{1-4}$ alkyl(SO) $C_{0-4}$ alkyl,  $C_{1-4}$ alkyl(SO) $C_{0-4}$ alkyl,  $C_{1-4}$ alkyl, (SO) $C_{0-4}$ alkyl, (SO) $C_{0-4}$ alkyl, OC $_{1-4}$ alkyl, C $_{1-4}$ alkylOR $_{1-4}$ AlkylOR

Q is selected the group consisting of heterocycloalkyl and heteroaryl;

R<sup>2</sup> and R<sup>3</sup> are independently selected from the group consisting of: hydroxy, C<sub>0-6</sub>alkylcyano, oxo, =NR<sup>5</sup>, =NOR<sup>5</sup>, C<sub>1-4</sub>alkylhalo, halo, C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, C<sub>0-6</sub>alkylaryl, C<sub>0-6</sub>alkylheteroaryl, C<sub>1-6</sub>alkylcycloalkyl, C<sub>0-6</sub>alkylheterocycloalkyl, OC<sub>1-4</sub>alkyl, OC<sub>0-6</sub>alkylaryl, O(CO)C<sub>1-4</sub>alkyl, (CO)OC<sub>1-4</sub>alkyl, C<sub>0-4</sub>alkyl(SO)C<sub>0-4</sub>alkyl, C<sub>1-4</sub>alkyl(SO<sub>2</sub>)C<sub>0-4</sub>alkyl, (SO)C<sub>0-4</sub>alkyl, (SO<sub>2</sub>)C<sub>0-4</sub>alkyl, C<sub>1-4</sub>alkylOR<sup>5</sup>, C<sub>0-4</sub>alkylNR<sup>5</sup>R<sup>6</sup> and a 5- or 6-membered ring containing atoms independently selected from C, N, O and S, which ring may optionally be fused with a 5- or 6-membered ring containing atoms independently selected from the group consisting of C, N and O and wherein said ring and said fused ring may be substituted by one or more A;

wherein any  $C_{1-6}$ alkyl, aryl, or heteroaryl defined under  $R^1$ ,  $R^2$  and  $R^3$  may be substituted by one or more A;

A is selected from the group consisting of: hydrogen, hydroxy, halo, nitro, oxo,  $C_{0-6}$ alkylcyano,  $C_{0-4}$ alkyl $C_{3-6}$ cycloalkyl,  $C_{1-6}$ alkyl,  $-OC_{1-6}$ alkyl,  $C_{1-6}$ alkylhalo,  $OC_{1-6}$ alkylhalo,  $C_{2-6}$ alkenyl,  $C_{0-3}$ alkylaryl,  $C_{0-6}$ alkyl $OR^5$ ,  $OC_{2-6}$ alkyl $OR^5$ , O

 $R^5$  and  $R^6$  are independently selected from, H,  $C_{1\text{-}6}$ alkyl,  $C_{3\text{-}7}$ cycloalkyl and aryl;

m is selected from 0, 1, 2, 3 or 4;

n is selected from 0, 1, 2, 3 or 4;

p is selected from 0, 1, 2, 3 or 4; and

a salt or hydrate thereof,

with the proviso that the compound is not:

4,4'-(1,2-piperazinediyl)di-antipyrine;

4,4'-(1,2-piperazinediyl)di-antipyrine dihydrochloride; or

- 4,4'-(1,2-piperazinediyl)di-antipyrine dipicrate;
- 2. (Original) A compound according to claim 1 wherein m is selected from 1, 2, 3 or 4
- 3. (Original) A compound according to claim 1 wherein  $X^7$  is C.
- 4. (Original) A compound according to claim 1 wherein X<sup>5</sup> is selected from the group consisting of CR<sup>4</sup>R<sup>4</sup>, NR<sup>4</sup>, O, S, SO and SO<sub>2</sub>.
- 5. (Original) A comound according to claim 1 wherein  $X^3$  is selected from the group consisting of N and O.
- 6. (Original) A compound according to claim 1 wherein P is aryl.
- 7. (Original) A compound according to claim 6 wherein P is phenyl.
- 8. (Original) A compound according to claim 7 wherein m is selected from the group consisting of 1 and 2.

- 9. (Original) A compound according to claim 1 wherein R<sup>1</sup> is selected from the group consisting of: halo, C<sub>1-6</sub>alkylhalo, OC<sub>1-6</sub>alkylhalo, C<sub>1-6</sub>alkyl, OC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylOR<sup>5</sup>, C<sub>0-6</sub>alkylNR<sup>5</sup>R<sup>6</sup>.
- 10. (Original) A compound according to claim 9 wherein R<sup>1</sup> is selected from the group consisting of: Cl, F, Me, OMe, CF<sub>3</sub>, OCF<sub>3</sub>, and CN.
- 11. (Original) A compound according to claim 1 wherein  $X^2$  is C.
- 12. (Original) A compound according to claim 11 wherein X<sup>1</sup> is N or CR<sup>4</sup>.
- 13. (Original) A compound according to claim 12 wherein when  $X^3$  is O,  $X^4$  is N and when  $X^3$  is N,  $X^4$  is O.
- 14. (Original) A compound according to claim 1 wherein  $X^2$  is N.
- 15. (Original) A compound according to claim 14 wherein  $X^1$  is N.
- 16. (Original) A compound according to claim 15 wherein  $X^3$  is N and  $X^4$  is N or  $CR^4$ .

7

- 17. (Original) A compound according to claim 1 wherein  $X^6$  is N.
- 18. (Original) A compound according to claim 12 wherein  $X^5$  is selected from the group consisting of a bond,  $CR^4R^4$ ,  $NR^4$  and O.
- 19. (Original) A compound according to claim 13 wherein  $X^5$  is selected from the group consisting of a bond, O and  $NR^4$ .
- 20. (Original) A compound according to claim 16 wherein  $X^5$  is selected from the group consisting of O and  $CR^4$ .
- 21. (Original) A compound according to claim 1 wherein  $R^4$  is selected from the group consisting of: hydrogen,  $C_{1-6}$ alkyl,  $C_{1-6}$ alkylhalo and halo.
- 22. (Original) A compound according to claim 1 wherein Q is heteroaryl.
- 23. (Original) A compound according to claim 1 wherein Q is selected from the group consisting of:

$$X^{6}$$
,  $X^{6}$ ,  $X$ 

24. (Original) A compound according to claim 23 wherein Q is

- 25. (Original) A compound according to claim 1 wherein  $R^2$  and  $R^3$  are independently selected from the group consisting of:  $C_{1-4}$ alkylhalo,  $C_{1-6}$ alkyl,  $C_{3-6}$ cycloalkyl,  $C_{0-6}$ alkylaryl and  $C_{0-6}$ alkylheteroaryl.
- 26. (Original) A compound according to claim 1 wherein A is selected from the group consisting of: hydrogen, hydroxyl, halo, C<sub>0-6</sub>alkylcyano, C<sub>1-6</sub>alkyl, -OC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylhalo, OC<sub>1-6</sub>alkylhalo.
- 27. (Original) A compound according to claim 1 selected from:

  4-(5-{2-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-piperidin-1-yl}-4-methyl-4H [1,2,4]triazol-3-yl)pyridine

9

3-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-4-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-morpholine

3-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-4-[5-(4-difluoromethoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-yl]-morpholine

3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-4-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-morpholine

3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-4-[5-(4-difluoromethoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-yl]-morpholine

3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-4-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-piperazine-1-carboxylic acid tert-butyl ester

2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-(4-methyl-5-pyridin-4-yl-4H-1,2,4]triazol-3-yl)-piperazine

2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-4-methyl-1-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-piperazine

3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-4-[5-(4-difluoromethoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-yl]-piperazine-1-carboxylic acid tert-butyl ester

2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-[5-(4-difluoromethoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-yl]-piperazine

2-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-1-[5-(4-difluoromethoxy-phenyl)-4-methyl-4H-[1,2,4]triazol-3-yl]-4-methyl-piperazine

2-[2-(3-Chlorophenyl)-2H-tetrazol-5-yl]-1-{5-[4-(difluoromethoxy)phenyl]-4-methyl-4H-1,2,4-triazol-3-yl}piperidine

4-(5-{2-[2-(3-chlorophenyl)-2H-tetrazol-5-yl]piperidin-1-yl}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine

2-[2-(3-Chlorophenyl)-2H-tetrazol-5-yl]-1-[5-(4-methoxyphenyl)-4-methyl-4H-1,2,4-triazol-3-yl]piperidine

[4-(5-{2-[2-(3-chlorophenyl)-2H-tetrazol-5-yl]piperidin-1-yl}-4-methyl-4H-1,2,4-triazol-3-yl)phenyl]dimethylamine

[4-(5-{2-[2-(3-Chloro-phenyl)-2H-tetrazol-5-yl]-piperidin-1-yl}-4-methyl-4H-[1,2,4]triazol-3-yl)-benzyl]-dimethyl-amine

{2-[4-(5-{2-[2-(3-Chloro-phenyl)-2H-tetrazol-5-yl]-piperidin-1-yl}-4-methyl-4H-[1,2,4]triazol-3-yl)-phenoxy]-ethyl}-dimethyl-amine

- (R)-3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-4-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-morpholine
- (S) 3-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-4-(4-methyl-5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-morpholine
- (R)-2-[2-(3-Chlorophenyl)-2H-tetrazol-5-yl]-1-{5-[4-(difluoromethoxy)phenyl]-4-methyl-4H-1,2,4-triazol-3-yl}piperidine
- (S)-2-[2-(3-Chlorophenyl)-2H-tetrazol-5-yl]-1-{5-[4-(difluoromethoxy)phenyl]-4-methyl-4H-1,2,4-triazol-3-yl}piperidine

(R)-4-(5-{2-[2-(3-Chlorophenyl)-2H-tetrazol-5-yl]piperidin-1-yl}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine

(S)-4-(5-{2-[2-(3-Chlorophenyl)-2H-tetrazol-5-yl]piperidin-1-yl}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine

4-[5-(5-{2-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-pyrrolidin-1-yl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-yl]-morpholine,

4-[5-(5-{2-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-pyrrolidin-1-yl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridin-2-yl]-morpholine,

3-(5-{2-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-pyrrolidin-1-yl}-4-methyl-4H-[1,2,4]triazol-3-yl)-pyridine,

4-(5-{2-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-pyrrolidin-1-yl}-4-cyclopropyl-4H-[1,2,4]triazol-3-yl)-pyridine,

3-[5-(3-Chloro-phenyl)-[1,2,4]oxadioazol-3-yl]-4-(5-pyridin-4-yl-4H-[1,2,4]triazol-3-yl)-morpholine,

3-[5-(3-chlorophenyl)isoxazol-3-yl]-4-(4- cyclopropyl-5-pyridin-3-yl-4H-1,2,4-triazol-3-yl)morpholine,

3-[5-(3-chlorophenyl)isoxazol-3-yl]-4-(4- cyclopropyl -5-pyridin-4-yl-4H-1,2,4-triazol-3-yl)morpholine,

3-[5-(3-chlorophenyl)isoxazol-3-yl]-4-(4-methyl-5-pyridin-3-yl-4H-1,2,4-triazol-3-yl)morpholine,

- 3-[5-(3-Chloro-phenyl)-isoxazol-3-yl]-4-[5-(6-methoxy-pyridin-3-yl)-4-methyl-4H-[1,2,4]triazol-3-yl]-morpholine,
- 3-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]-4-[5-(2-methoxypyridin-4-yl)-4-methyl-4H-1,2,4-triazol-3-yl]morpholine,
- 3-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]-4-[5-(2-methylpyridin-4-yl)-4-methyl-4H-1,2,4-triazol-3-yl]morpholine,
- 3-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]-4-[5-(5-fluoropyridin-3-yl)-4-methyl-4H-1,2,4-triazol-3-yl]morpholine,
- 3-[5-(3-chlorophenyl)isoxazol-3-yl]-4-[5-(5-fluoropyridin-3-yl)-4-methyl-4H-1,2,4-triazol-3-yl]morpholine,
- 3-[3-(3-chlorophenyl)-1,2,4-oxadiazol-5-yl]-4-(4-methyl-5-pyridin-2-yl-4H-1,2,4-triazol-3-yl)morpholine,
- 4-[5-(5-fluoropyridin-3-yl)-4-methyl-4H-1,2,4-triazol-3-yl]-3-[3-(3-iodophenyl)-1,2,4-oxadiazol-5-yl]morpholine,
- 3-[3-(3-iodophenyl)-1,2,4-oxadiazol-5-yl]-4-(4-methyl-5-pyridin-4-yl-4H-1,2,4-triazol-3-yl)morpholine,
- 3-[5-(3-chlorophenyl)isoxazol-3-yl]-4-[5-(2-methylpyridin-4-yl)-4-methyl-4H-1,2,4-triazol-3-yl]morpholine,
- 3-[2-(3-chlorophenyl)-2H-tetrazol-5-yl]-4-(4-methyl-5-pyridin-3-yl-4H-1,2,4-triazol-3-yl)morpholine,

3-[2-(3-chlorophenyl)-2H-tetrazol-5-yl]-4-[5-(3,5-difluorophenyl)-4-methyl-4H-1,2,4-triazol-3-yl]morpholine,

3-(5-{2-[5-(3-chlorophenyl)isoxazol-3-yl]pyrrolidin-1-yl}-4-cyclopropyl-4H-1,2,4-triazol-3-yl)pyridine, and

4-(5-{2-[5-(3-chlorophenyl)isoxazol-3-yl]pyrrolidin-1-yl}-4-methyl-4H-1,2,4-triazol-3-yl)pyridine.

28. (Original) A pharmaceutical composition comprising as active ingredient a therapeutically effective amount of the compound according to any one of claims 1 to 26, in association with one or more pharmaceutically acceptable diluent, excipients and/or inert carrier.

## 29. (CANCELLED)

- 30. (Currently Amended) The compound according to any one of claims 1 to 27 claim 1, for use in therapy.
- 31. (Currently Amended) The compound according to any one of claims 1 to 27 claim 1, for use in treatment of mGluR 5 mediated disorders.

- 32. (Currently Amended) Use of the compound according to any one of claims 1 to 27 claim

  1, in the manufacture of a medicament for the treatment of mGluR 5 mediated disorders.
- 33. (Currently Amended) A method of treatment of mGluR 5 mediated disorders, comprising administrering to a mammal, including man in need of such treatment, a therapeutically effective amount of the compound according to any one of claims 1 to 27 claim 1.
- 34. (Original) The method according to claim 33, for use in treatment of neurological disorders.
- 35. (Original) The method according to claim 33, for use in treatment of psychiatric disorders.
- 36. (Original) The method according to claim 33, for use in treatment of chronic and acute pain disorders.
- 37. (Original) The method according to claim 33, for use in treatment of gastrointestinal disorders.

Application No.: NEW Docket No.: 5999-0525PUS3

38. (Original) A method for inhibiting activation of mGluR 5 receptors, comprising treating a cell containing said receptor with an effective amount of the compound according to claim 1.